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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,494	11/13/2003	Doris Brugger	21487	8326

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,494	BRUGGER ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *7-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :2/12/04, 5/21/04, 7/29/04, 12/3/04.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-6 and 11-13, in the reply filed on 8/24/2006 is acknowledged. The traversal is on the ground(s) that searching all inventions of the instant application would not constitute an undue burden to the USPTO. This is not found persuasive because, as set forth in the requirement for restriction mailed on 5/22/2006, the subject matter of the instant application is drawn to products represented by PEG-modified polypeptides, and methods drawn to biochemical/analytical methods. Thus, the search required for the invention of group I would be different from the search required for the biochemical/analytical methods of group II.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicant's election with traverse of PEG-Lys31, in the reply filed on 8/24/2006 is acknowledged. The traversal is on the ground(s) that a search for lysine pegylated interferon (IFN)-α would uncover expose any prior art that might disclose any of the nine possible lysine points of attachment, and therefore searching the claims of group I would not pose a serious search burden.

These arguments have been fully considered and have been found to be persuasive. Therefore, the requirement for restriction regarding specific pegylated lysine residues, as set forth on pages 2-3 of the requirement for restriction mailed on 5/22/2006, is withdrawn.

3. Therefore, claims 1-13 are currently pending. Claims 7-10 are withdrawn as non-elected subject matter, and claims 1-6 and 11-13 are the subject of this office action.

Information Disclosure Statement

The information disclosure statements received on 2/12/2004, 5/21/2004, 7/29/2004, and 12/03/2004 have been fully considered by the Examiner.

Drawings

The drawings received on 7/9/2004 are objected to for the reasons set forth on form PTO-948.

Specification

1. The use of the trademarks TOYOPEARL® and VOYAGER-DE® has been noted in this application (paragraphs 0042 and 0053, respectively). Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

2. The specification is objected to because the description of the figures is not consistent with the figure labels. Specifically, several figures contain multiple parts (e.g. Figure 2A and 2B, Figure 3A, 3B, etc), which are not specifically described in the specification. Appropriate correction is required.

Claim Objections

1. Claim 1 is objected to because it recites "A positional isomers", and thus recites a product in both the singular ("A positional") and plural "isomers") forms.

2. Claim 6 is objected to for the following informality: The claim recites "claim3", and should be amended to recite "claim 3".

3. Claim 11 is objected to for the following informality: The claim has two periods at the end of the sentence.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it

is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition for the treatment of hepatitis C (HCV) infection, does not reasonably provide enablement for a composition for treatment of all other possible viral diseases or immunomodulatory diseases, and does not reasonably provide enablement for a composition for prophylaxis of any disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The claims of the instant invention are drawn to a pharmaceutical composition for the treatment or prophylaxis of viral or immunomodulatory diseases comprising an effective amount of a positional isomer of pegylated IFN-α2a. The term "prophylaxis" is not specifically defined by the specification, and is understood in the art to mean "prevention". The breadth of the claims is therefore excessive because given the broadest reasonable interpretation, the claims read on a pharmaceutical composition that can prevent all possible viral or immunomodulatory diseases in all possible patient populations. The specification does not provide guidance or examples of any viral or immunomodulatory disease that can be prevented, in any or all possible patient populations, by administration of a pharmaceutical composition comprising a positional isomer of pegylated IFN-α2a. A person of ordinary skill in the art would know that viral diseases such as hepatitis C (HCV) infection can be treated by administration of IFN-α2a (see Bailon *et al* – cited in the information disclosure statement received on 5/21/2004), but this treatment is not always effective for all patients. Given this uncertain efficacy of treating HCV infection with IFN-α2a-based therapies, one of ordinary skill in the art would certainly not be able to predict how to *prevent* HCV infection, or any other viral infection, with an IFN-α2a-based therapy such as administration of a positional isomer of IFN-α2a of the instant application.

Furthermore, the term "immunomodulatory" is broad and is not defined by the claims or the specification. There is no guidance in the specification that would enable a skilled artisan to treat or prevent all possible "immunomodulatory" diseases with a composition comprising a positional isomer of pegylated IFN-α2a, nor is there any example of any "immunomodulatory" disease that can be treated, much less prevented. Given the broadest reasonable interpretation, an "immunomodulatory disease" could be any disease in which immune functions are different, in any way and by any degree, from normal immune function, or any disease in which the immune system plays any role in the pathology of the disease. A person of ordinary skill in the art would be aware that IFN-α2a is used for treatment of HCV infection (see above). However, because a person of ordinary skill in the art would be aware of the uncertainties of IFN-α2a efficacy in treating viral diseases, such as HCV infection, in all possible patients, and also because the term "immunomodulatory disease" encompasses a large number of diseases, one of skill in the art would not be able to predict which "immunomodulatory" diseases, other than HCV infection, and other diseases known in the art to be responsive to IFN-α2a treatment, could be treated or prevented using the positional isomers of the instant invention.

Therefore, due to the excessive breadth of the claims, which read on a composition for prevention of all possible viral diseases, or treatment or prevention of all possible "immunomodulatory" diseases, the lack of guidance or examples showing that all viral diseases can be prevented with the claimed composition, or any immunomodulatory disease can be prevented or treated with the claimed composition, the unpredictability inherent in the art regarding the efficacy of IFN-α2a-based therapy for treating or preventing all possible viral or immumnomodulatory disease, a person of ordinary skill in the art would require further, undue experimentation to make and use a pharmaceutical composition that is commensurate in scope with the claims.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards

as the invention. The claims are drawn to a pharmaceutical composition for the treatment or prophylaxis of viral or immunomodulatory diseases. The metes and bounds of the term "immunomodulatory" are not defined by the specification or the claims, and the term is also not an art-accepted term for a class of diseases. Furthermore, even if the term was known in the art, the degree or type of "immunomodulation" that is characteristic of such diseases is not defined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-6 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Bailon *et al* (cited in the information disclosure statement received on 5/21/2006). The claims of the instant invention are drawn to a positional isomer of pegylated IFN-α2a, wherein the IFN-α2a is pegylated on a lysine residue selected from Lys31, Lys49, Lys70, Lys83, Lys112, Lys121, Lys131, Lys134, or Lys164. The claims are further drawn to a positional isomer of pegylated IFN-α2a wherein the average molecular weight of the polyethylene glycol (PEG) moiety is about 40,000 daltons, and a pharmaceutical composition comprised of a positional isomer of pegylated IFN-α2a.

Bailon *et al* teaches IFN-α2a isomers that are monopegylated lysine residues, and specifically teaches IFN-α2a monopegylated on Lys31, Lys121, Lys131, and Lys134 (see abstract, and page 198, 1st column, 1st full paragraph). Bailon *et al* also discloses that the PEG moiety that is attached to the various lysine residues has a molecular weight of 40,000 daltons (see abstract; page 197, 1st column – results section, and Figure 1). Furthermore, Bailon *et al* teaches administration of pegylated IFN-α2a isomers in a sterile buffer (page 196, 2nd column, 1st paragraph; page 198 2nd column – page 199, 1st column, and Figures 4 and 5). Thus, by

teaching positional isomers of IFN-α2a pegylated at Lys31, Lys121, Lys131, and Lys134, wherein the PEG is 40,000 daltons, and the pegylated isomers used in a pharmaceutical composition comprised of a sterile buffer for in vivo administration, Bailon *et al* meets the limitations of claims 1-6 and 11-13 of the instant invention.

2. Claims 1-3 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Monkarsh *et al* (cited in the information disclosure statement received on 2/12/2004). The subject matter of the claims of the instant invention is discussed *supra.*

Monkarsh *et al* discloses several positional isomers of monopegylated IFN-α2a, and specifically teaches IFN-α2a monopegylated at Lys31, Lys49, Lys70, Lys83, Lys112, Lys121, Lys131, Lys134, and Lys164 (page 438-439, and Table 1), thus meeting the limitations of claims 1-3. Furthermore, Monkarsh *et al* describes administration of the various pegylated IFN-α2a positional isomers to tissue culture cells (see page 439, Table 2). Although Monkarsh *et al* does not specifically disclose a pharmaceutical composition comprised of the various pegylated IFN-α2a isomers, it would be expected, in the absence of evidence to the contrary, that because the various isomers exhibited biological activity (see Table 2), they were administered in a pharmaceutically acceptable form, such as a physiological buffer. Thus, Monkarsh *et al* also meets the limitations of claims 11-13.

3. Claims 1-3 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Gilbert *et al* (US 5,951,974). The subject matter of the claims of the instant invention is discussed *supra.*

Gilbert *et al* discloses positional isomers of pegylated IFN-α2a, wherein said pegylation is on Lys31, Lys49, Lys83, Lys121, Lys131, and Lys134 (column 6, lines 50-57; claims 7-8), thus meeting the limitations of claims 1-3 of the instant application. Furthermore, the polypeptides taught by Gilbert *et al* can be incorporated in a pharmaceutical formulation or composition comprising an effective amount of the IFN-α2a positional isomer and a pharmaceutically acceptable carrier (column 11, lines 3-17). Therefore, Gilbert *et al* also meets the limitations of claims 11-13.

4. Claims 1-6 and 11-13 rejected under 35 U.S.C. 102(e) as being anticipated by Barker et al (US 2004/0136955 A1). The subject matter of the claims of the instant invention is discussed *supra*.

Barker *et al* discloses modified IFN polypeptides, including IFN-α2a (see paragraph 0010). Specifically, Barker *et al* teaches modification of IFN-α polypeptides by pegylation, including pegylation with PEG moieties having a molecular weight of about 40,000 daltons (see paragraphs 0017, 0079), and pegylation of IFN-α at lysine residues, such as Lys31, Lys49, Lys70, Lys83, Lys112, Lys121, Lys131, Lys134, and Lys164 (see paragraph 0080). Thus, by teaching pegylation of IFN-α2a at various lysine residues, including those listed in claim 1, and pegylation with a PEG moiety having a molecular weight of 40,000 daltons, Barker *et al* meets the limitations of claims 1-6. Barker *et al* also teaches pharmaceutical compositions comprised of modified/pegylated IFN polypeptides (see paragraphs 0099 – 0118), thus meeting the limitations of claims 11-13.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

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